Kolloquium „Statistische Methoden in der empirischen Forschung“

Wann: 04. Februar 2014, 17:00 – 18:30 Uhr

Wo: Landwirtschaftlich-Gärtnerische Fakultät der HU, Hörsaal 2, 2. Etage, Invalidenstr. 42, 10115 Berlin

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A guide to adjusting survival time estimates to account for treatment switching in randomized controlled trials

OBJECTIVES
Treatment switching is a common issue in clinical trials of cancer treatments – often patients randomised to the control group are permitted to switch onto the experimental treatment at some point during follow-up. In such circumstances an intention to treat (ITT) analysis will result in biased estimates of the overall survival advantage – and therefore the cost-effectiveness – associated with the experimental treatment. Methods to adjust for switching have been used inconsistently and potentially inappropriately in health technology assessments (HTA).

We present an analytical framework to guide analysts on the use of methods to adjust for treatment switching in the context of economic evaluations.

METHODS
We conducted a review of methods used to adjust for treatment switching in HTA, and two rigorous simulation studies to assess the performance of adjustment methods in a range of realistic scenarios. We tested different simulated trial sample sizes, crossover proportions, treatment effect sizes, levels of administrative censoring, and data generating models. Combining the findings from our review and our simulation study, we made practical recommendations on the use of adjustment methods in HTA.

RESULTS
Our review demonstrates that adjustment methods make important limiting assumptions. Our simulation studies show that the bias associated with alternative methods is highly associated with deviations from their assumptions. Our recommended analysis framework aims to help researchers find suitable adjustment methods on a case-by-case basis. The characteristics of clinical trials and the treatment switching mechanism observed within them, should be considered alongside the key assumptions of the adjustment methods.

CONCLUSIONS
The limitations associated with switching adjustment methods mean that different methods are appropriate in different scenarios. In some scenarios all methods may be prone to important bias. The data requirements of adjustment methods have important implications for people who design and analyse trials which allow treatment switching.